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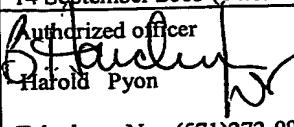
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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BU-131XQ999		FOR FURTHER ACTION	See Form PCT/IPEA/416																								
International application No. PCT/US04/31177		International filing date (day/month/year) 23 September 2004 (23.09.2004)	Priority date (day/month/year) 23 September 2003 (23.09.2003)																								
International Patent Classification (IPC) or national classification and IPC IPC(7): B32B 3/00,3/28,3/30,27/00,27/32; C12Q 1/00 and US Cl.: 428/156,166,167,500,523; 435/4																											
Applicant TRUSTEES OF BOSTON UNIVERSITY																											
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of <u>10</u> sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																											
<p>4. This report contains indications relating to the following items:</p> <table> <tbody> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </tbody> </table>				<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand 15 July 2005 (15.07.2005)		Date of completion of this report 14 September 2005 (14.09.2005)																									
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		<p>Authorized officer  Harold Pyon</p> <p>Telephone No. (571)272-0987</p>																									

Form PCT/IPEA/409 (cover sheet)(April 2005)

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/US04/31177

Box No. I Basis of the report

1. With regard to the language, this report is based on:

the international application in the language in which it was filed.

a translation of the international application into English, which is the language of a translation furnished for the purposes of:

- international search (under Rules 12.3 and 23.1(b))
- publication of the international application (under Rule 12.4(a))
- international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

the international application as originally filed/furnished

the description:

pages 1-31 as originally filed/furnished

pages* NONE received by this Authority on _____

pages* NONE received by this Authority on _____

the claims:

pages NONE as originally filed/furnished

pages* NONE as amended (together with any statement) under Article 19

pages* 32-33H received by this Authority on 15 JULY 2005

pages* NONE received by this Authority on _____

the drawings:

pages 1/12-12/12 as originally filed/furnished

pages* NONE received by this Authority on _____

pages* NONE received by this Authority on _____

a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. The amendments have resulted in the cancellation of:

the description, pages _____

the claims, Nos. 1-9 _____

the drawings, sheets/figs _____

the sequence listing (specify): _____

any table(s) related to the sequence listing (specify): _____

4. This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

the description, pages _____

the claims, Nos. _____

the drawings, sheets/figs _____

the sequence listing (specify): _____

any table(s) related to the sequence listing (specify): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/31177

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>10-50</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>10-50</u>	NO
Industrial Applicability (IA)	Claims <u>10-50</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and Explanations (Rule 70.7)

Claims 10-50 lack novelty under PCT Article 33(2) as being anticipated by Morgan et al. Morgan et al. teaches the claimed three-dimensional hydrogel structure including the first hydrogel, a micropattern defining a surface of the first hydrogel, the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the first hydrogel and a second hydrogel operably interfaced with the first hydrogel, wherein the second hydrogel has a micropattern defining a surface of the second hydrogel, the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the second hydrogel.

Claims 10-50 lack novelty under PCT Article 33(2) as being anticipated by Everhart et al. Everhart et al. teaches the claimed three-dimensional hydrogel structure including the first hydrogel, a micropattern defining a surface of the first hydrogel, the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the first hydrogel and a second hydrogel operably interfaced with the first hydrogel, wherein the second hydrogel has a micropattern defining a surface of the second hydrogel, the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the second hydrogel.

Claims 10-50 lack novelty under PCT Article 33(2) as being anticipated by Kim. Kim teaches the claimed three-dimensional hydrogel structure including a polymer array of a hydrogel, the polymer array comprising a fluid, wherein the fluid hydrates the polymer array; and a micropattern defining a surface of the hydrogel, the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogel.

Claims 10-50 have industrial applicability as defined by PCT Article 33(4) since the claimed three-dimensional hydrogel can be made and/or used in bioengineering and medicine.

----- NEW CITATIONS -----

NONE

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CLAIMS

What is claimed is:

1. (Canceled)

5

2. (Canceled)

3. (Canceled)

10 4. (Canceled)

5. (Canceled)

6. (Canceled)

15

7. (Canceled)

8. (Canceled)

20 9. (Canceled)

10. (New) A three-dimensional hydrogel structure micropatterned by a mold from which the hydrogel structure has been separated, the hydrogel structure comprising:

25 a polymer array of a hydrogel, the polymer array comprising a fluid that hydrates the polymer array and a second hydrogel comprising a second polymer array hydrated by a second fluid; and
a micropattern defining a surface of at least one hydrogel, the micropattern corresponding to an inverse micropattern transferred
30 from a mold after separation of the mold from the hydrogels.

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11. (New) The three-dimensional hydrogel structure of claim 10, wherein the hydrogel comprises a cavity, whereby the cavity is formed by perturbing a portion of the second hydrogel.
- 5 12. (New) The three-dimensional hydrogel structure of claim 11, wherein an enzyme perturbs the portion of the second hydrogel by digesting the portion.
- 10 13. (New) The three-dimensional hydrogel structure of claim 11, wherein the portion of the second hydrogel is perturbed by a change in temperature.
- 15 14. (New) The three-dimensional hydrogel structure of claim 10, wherein the mold substantially comprises silicon materials, poly(dimethylsiloxane) materials, photoresist materials, glass materials, plastic materials, rubber materials, synthetic materials, polymer materials, organic materials or any combination thereof.
- 20 15. (New) The three-dimensional hydrogel structure of claim 10, wherein the polymer array further comprises materials selected from the group consisting of biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations thereof.
- 25 16. (New) The three-dimensional hydrogel structure of claim 11, wherein the cavity is contacted by flow of a liquid.
- 30 17. (New) The three-dimensional hydrogel structure of claim 16, wherein the liquid comprises materials that are selected from the group consisting of biological components, organic components, metallic components, cellular components, synthetic

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components, intact cells, inorganic components and combinations thereof.

18. (New) The three-dimensional hydrogel structure of claim 17,
5 wherein the materials of the liquid adhere to a portion of the cavity.

19. (New) A three-dimensional hydrogel structure micropatterned by a mold from which the hydrogel structure has been separated, the
10 hydrogel structure comprising:

a polymer array of a hydrogel, the polymer array comprising a fluid that hydrates the polymer array, wherein the hydrogel is interfaced with a precursor of a second hydrogel comprising a second polymer array hydrated by a second fluid, whereby the precursor of the second hydrogel diffuses into the hydrogel interfaced therewith to adhere the hydrogels as the second hydrogel forms; and

20 a micropattern defining a surface of at least one hydrogel, the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels.

25 20. (New) A three-dimensional hydrogel structure micropatterned by a mold from which the hydrogel structure has been separated, the hydrogel structure comprising:

a polymer array of a hydrogel, the polymer array comprising a fluid that hydrates the polymer array, wherein the hydrogel is interfaced with a second hydrogel comprising a second polymer array hydrated by a second fluid, whereby a destabilizer contacting the hydrogel and the second hydrogel conforms at least one of the hydrogels to adhere the interfaced hydrogels together when a concentration of the destabilizer is reduced; and

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a micropattern defining a surface of at least one hydrogel, the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels.

5 21. (New) The three-dimensional hydrogel structure of claim 20, wherein the destabilizer is selected from the group consisting of chaotropes, kosmotropes, urea, glucose, glycerol, guanidinium hydrogen chloride and combinations thereof.

10 22. (New) The three-dimensional hydrogel structure of claim 20, wherein the concentration of the destabilizer is reduced when a stabilizer contacts the hydrogels.

15 23. (New) The three-dimensional hydrogel structure of claim 22, wherein the destabilizer and the stabilizer are selected from the group consisting of chaotropes, kosmotropes, urea, glucose, glycerol, guanidinium hydrogen chloride and combinations thereof.

20 24. (New) A three-dimensional hydrogel structure micropatterned by a mold from which the hydrogel structure has been separated, the hydrogel structure comprising:

25 a polymer array of a hydrogel, the polymer array comprising a fluid that hydrates the polymer array and a second hydrogel comprising a second polymer array hydrated by a second fluid, whereby precursors of the hydrogel and the second hydrogel were combined to interface the hydrogels as at least one hydrogel is formed; and

30 a micropattern defining a surface of at least one hydrogel, the micropattern corresponding to an inverse micropattern transferred from a mold after separation of the mold from the hydrogels.

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25. (New) The three-dimensional hydrogel structure of claim 24,
wherein the precursor of the hydrogel or second hydrogel
comprises a material selected from the group consisting of
biological components, organic components, metallic components,
5 cellular components, synthetic components, intact cells,
inorganic components and combinations thereof.

26. (New) The three-dimensional hydrogel structure of claim 19,
20 or 24, wherein the hydrogel and second hydrogel form a
10 network.

27. (New) The three-dimensional hydrogel structure of claim 26,
wherein the network is contacted by flow of a liquid.

15 28. (New) The three-dimensional hydrogel structure of claim 27,
wherein the liquid comprises materials that are selected from
the group consisting of biological components, organic
components, metallic components, cellular components, synthetic
components, intact cells, inorganic components and combinations
20 thereof.

29. (New) The three-dimensional hydrogel structure of claim 28,
wherein the materials of the liquid adhere to a portion of the
network.

25 30. (New) The three-dimensional hydrogel structure of claim 10,
19, 20 or 24, wherein a portion of at least one hydrogel is
interfaced with a substrate.

30 31. (New) A method for micropatterning a three-dimensional hydrogel
structure, the method comprising:
providing a mold, the mold comprising a micropatterned
surface;

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treating the micropatterned surface of the mold with a release agent;

5 forming a hydrogel from a precursor, wherein the precursor is in contact with the treated micropatterned surface of the mold while the hydrogel is formed, the hydrogel comprising a fluid that hydrates a polymer array and a second hydrogel comprising a second polymer array hydrated by a second fluid; and

10 separating the hydrogels from the treated micropatterned surface of the mold such that the mold transfers an inverse of a micropattern to a surface of at least one hydrogel.

32. (New) The method of claim 31, the method further comprising forming a cavity within the hydrogel by perturbing a portion of 15 the second hydrogel.

33. (New) The method of claim 32, wherein an enzyme perturbs the portion of the second hydrogel by digesting the portion.

20 34. (New) The method of claim 32, wherein the portion of the second hydrogel is perturbed by a change in temperature.

35. (New) The method of claim 31, wherein the polymer array further comprises materials selected from the group consisting 25 of biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations thereof.

36. (New) The method of claim 32, the method further comprising flowing a liquid through the cavity.

37. (New) The method of claim 36, wherein the liquid comprises materials that are selected from the group consisting of

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biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations thereof.

5 38. (New) The method of claim 37, wherein the materials of the liquid adhere to a portion of the cavity.

39. (New) A method for micropatterning a three-dimensional hydrogel structure, the method comprising:

10 providing a mold, the mold comprising a micropatterned surface;

treating the micropatterned surface of the mold with a release agent;

15 forming a hydrogel from a precursor, wherein the precursor is in contact with the treated micropatterned surface of the mold while the hydrogel is formed, the hydrogel comprising a fluid that hydrates a polymer array;

interfacing the hydrogel with a precursor for a second hydrogel;

20 diffusing the precursor for the second hydrogel into the hydrogel interfaced therewith;

forming the second hydrogel to adhere the hydrogels; and

25 separating the hydrogels from the treated micropatterned surface of the mold such that the mold transfers an inverse of a micropattern to a surface of at least one hydrogel.

40. (New) A method for micropatterning a three-dimensional hydrogel structure, the method comprising:

providing a mold, the mold comprising a micropatterned surface;

treating the micropatterned surface of the mold with a release agent;

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forming a hydrogel from a precursor, wherein the precursor is in contact with the treated micropatterned surface of the mold while the hydrogel is formed, the hydrogel comprising a fluid that hydrates a polymer array;

5 interfacing the hydrogel with a second hydrogel;

conforming at least one of the interfaced hydrogels by contacting the hydrogels with a destabilizer;

reducing a concentration of the destabilizer to adhere the hydrogels together; and

10 separating the hydrogels from the treated micropatterned surface of the mold such that the mold transfers an inverse of a micropattern to a surface of at least one hydrogel.

41. (New) The method of claim 40, wherein the destabilizer is
15 selected from the group consisting of chaotropes, kosmotropes, urea, glucose, glycerol, guanidinium hydrogen chloride and combinations thereof.

42. (New) The method of claim 40, wherein the concentration of
20 the destabilizer is reduced when a stabilizer contacts the hydrogels.

43. (New) The method of claim 42, wherein the destabilizer and the stabilizer are selected from the group consisting of
25 chaotropes, kosmotropes, urea, glucose, glycerol, guanidinium hydrogen chloride and combinations thereof.

44. (New) A method for micropatterning a three-dimensional hydrogel structure, the method comprising:

30 providing a mold, the mold comprising a micropatterned surface;

treating the micropatterned surface of the mold with a release agent;

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..combining a precursor for a hydrogel with a precursor for a second hydrogel;

forming the hydrogels from the precursors, wherein the precursors are in contact with the treated micropatterned surface 5 of the mold while the hydrogels are formed; and

separating the hydrogels from the treated micropatterned surface of the mold such that the mold transfers an inverse of a micropattern to a surface of at least one hydrogel.

10 45. (New) The method of claim 44, wherein the precursor of the hydrogel or second hydrogel comprises a material selected from the group consisting of biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations 15 thereof.

46. (New) The method of claim 39, 40 or 44, wherein the hydrogel and second hydrogel form a network.

20 47. (New) The method of claim 46, the method further comprising contacting the network with flow of a liquid.

48. (New) The method of claim 47, wherein the liquid comprises materials that are selected from the group consisting of 25 biological components, organic components, metallic components, cellular components, synthetic components, intact cells, inorganic components and combinations thereof.

49. (New) The method of claim 48, wherein the materials of the 30 liquid adhere to a portion of the network.

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50. (New) The method of claim 31, 39, 40 or 44, the method further comprising interfacing a portion of at least one hydrogel with a substrate.

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